REMARKS

In the specification, the paragraphs beginning at page 19, line 20; page 21, line 27; page 24, line 3; and page 31, line 25 have been amended to properly identify trademarked terms.

Claims 11, 12, 21, 23-29, and 31 remain in this application. Claims 1-10, 13-20, 22, and 30 have been cancelled without prejudice.

REJECTIONS UNDER 35 U.S.C. § 102

The Examiner has rejected claims 11 and 12 as allegedly anticipated by U.S. Patent No. 5,150,328. The Examiner contends that the '328 patent describes the administration of BMP-2 to treat bone and cartilage defects, and that this administration would inherently result in inhibitory effects on IL-1. The Examiner also rejected claims 11 and 12 as allegedly anticipated by U.S. Patent No. 6,287,816. The Examiner contends that the '816 patent teaches administration of BMP-9 to treat cartilage, liver, and bone defects, and that this administration would inherently result in effects on IL-1. Applicants traverse.

Claim 11 recites administration of an effective amount of BMP for reducing IL-1 effects on cartilage tissue. To anticipate a claim under 35 U.S.C. § 102, the prior art must teach each and every limitation of the claim. The mere fact that the prior art may teach the production of a result within the scope of the claims is not sufficient for inherent anticipation. Instead, the Examiner must provide a basis in fact and/or technical reasoning to prove that the allegedly inherent characteristic necessarily flows from the teachings of the prior art. Manual of Patent Examining Procedure, Section

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

2112. There is no teaching or suggestion in the '328 or '816 patents that BMPs reduce IL-1's effect on cartilage tissue. There is no indication that IL-1 is involved at all in the methods described in the prior art. IL-1 causes cartilage damage. The cartilage tissue described in the '328 and '816 patents is not damages, thus, it is unlikely that IL-1 is active in that tissue. If IL-1 is not active in the tissue, then BMPs cannot reduce its activities.

Furthermore, Applicants' specification describes several situations where BMPs do not alter IL-1's effects on cartilage tissue. Figure 3A, lane 14, shows that 200 ng/ml of BMP-2 cannot reverse the effects of 200 pg/ml of IL-1. Figure 3C, lane 7, shows that 100 ng/ml of BMP-9 is ineffective in reducing the effects of 200 pg/ml of IL-1. Therefore, even in Applicants' own disclosure, the claimed results do not necessarily flow from administration of any amount of BMP. Thus, the pending claims, which require administration of an effective amount of BMP to inhibit or suppress the effects of IL-1, are novel. Neither the '328 patent nor the '816 patent describe how one would determine an effective amount of BMP for regulating IL-1 activity. It is only with the teachings of this application that one would understand that BMPs may have an effect on IL-1-induced cartilage damage, and only here is information provided as to the levels of BMP needed to alleviate IL-1 effects. Accordingly, the pending claims are not anticipated by the '318 or '816 patents. Applicants respectfully request that the Examiner withdraw this rejection.

The Examiner rejected has claims 21-31 as allegedly anticipated by WO 00/29552. The Examiner contends that WO 00/29552 describes an alginate layer system containing mesenchymal stem cells in alginate, and that these alginate systems

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

can be used for cartilage regeneration. The Examiner further contends that WO 00/29552 describes the use of BMP-2 in this system as an additional chondrogenic agent. Applicants traverse.

Applicants' claims recite methods for inducing chondrogenesis using non-expanded cells. The methods of claims 21-31 can only be practiced with non-expanded cells, while WO 00/29552 only describes tissue culture expanded cells. Applicants' invention provides the first description of the use of non-expanded cells for inducing chondrogenesis. Because WO 00/29552 does not describe the use of non-expanded cells, it does not teach all the limitations of the claims and therefore, cannot anticipate claims 21-31. Furthermore, claims 21, 26, 27, and 28 have been amended to recite a specific population of CD105+ cells, as opposed to general bone marrow or mesenchymal stem cells. Therefore, claims 21-31 now require that the cell population used in the methods express the CD105 surface molecule, which is not taught or even suggested in WO 00/29552. Applicants respectfully request that the Examiner withdraw this rejection of claims 21-31.

REJECTIONS UNDER 35 U.S.C. § 103

The Examiner rejected claims 21-31 as allegedly obvious over WO 00/29552 in view of the '816 patent, which refers to the use of BMP-9 to treat cartilage defects. The Examiner contends that it would be obvious to combine the teachings of WO 00/29552 and the '816 patent to co-administer BMP-9 with MSCs.

A prima facie case of obviousness under 35 U.S.C. § 103(a) has three requirements. First, there be some suggestion in the art itself to modify its teachings to

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
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reach the claimed invention. Second, the modification of the prior art must provide a reasonable expectation of success in producing the claimed invention. Finally, the suggested modification of the art must teach all the limitations of the claims. Manual of Patent Examining Procedure, Section 2143.

As set forth above, the MSCs described in WO 00/29552 are not the same as the CD105+ cells described and claimed in the pending application. The MSCs of WO 00/29552 were selected by adherence to tissue culture plates after several rounds of expansion. They are not all CD105+, and they possess different characteristics than the non-expanded CD105+ cells of Applicants' invention. Therefore, WO 00/29552, even when combined with the knowledge of the skilled artisan, does not teach all the limitations of the claims. Therefore, a prima facie case of obviousness cannot be established for WO 00/29552.

The '816 simply describes the use of BMP-9 for inducing cartilage growth. The teachings of WO 00/29552 are insufficient for establishing a case of obviousness for BMPs, and combination with the '816 patent does not remedy the defects in WO 00/29552. Therefore, the simple addition of information about BMP-9 activity will not render Applicants' invention any more obvious. Therefore, Applicants respectfully request that the Examiner withdraw this rejection of claims 21-31 as allegedly obvious.

Additionally, Applicants' invention has several unexpected advantages over the compositions of WO 00/29552. These advantages are described in Applicants' specification at page 8. First, adherence selection does not correlate with chondrogenic potential, whereas Applicants have demonstrated that the presence of CD105 on the cell surface does correlate with chondrogenic potential. Second, culture expansion may

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
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alter the cell surface characteristics of the cells, and create a greater likelihood for host response to the cells, while non-tissue culture expanded cells have no opportunity to alter surface protein expression patterns. And finally, the use of non-tissue culture expanded cells eliminates the time-consuming, expensive, and laborious process of multiple steps of tissue culture expansion.

These advantages were not recognized in WO 00/29552. The teachings of WO 00/29552 would not provide a reasonable expectation of success in practicing the current invention, nor would it provide any motivation to modify it's teachings to reach the current invention, because there was no suggestion of the methods of the invention at all, nor any indication that there were further solutions to the problem that were not solved by the invention described in WO 00/29552.]

REJECTIONS UNDER 35 U.S.C. § 112, 1ST PARAGRAPH

The Examiner has rejected claims 21-31 as allegedly lacking enablement. The Examiner contends that the specification allegedly does not enable all methods of promoting chondrogenesis using MSCs (claims 21-29) or all bone marrow cells (claims 21 and 26-28). The Examiner also contends that the specification does not enable repairing all tissue, as recited in claims 28-31.

The Examiner states that there is no evidence in the specification that non-expanded cells could be used to induce chondrogenesis without incorporation into a three dimensional structure, such as an alginate system. The Examiner also contends that the teachings regarding CD105+ cells are not predictive of the use of bone marrow cells in general. Finally, the Examiner contends that the teachings regarding the

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

induction of cartilage growth cannot be extrapolated to the claimed induction of tissue growth.

Claims 21 and 26-28 have been amended to recite that the non-tissue cultured expanded cells be CD105+ and to recite that the CD105+ cells be administered along with a suitable matrix carrier. Claim 28 has been amended to indicate that the repaired tissue is cartilage tissue. The amended claims are commensurate in scope with the teachings of the specification, and are therefore claims allowable under 35 U.S.C. § 112, first paragraph. Accordingly, Applicants respectfully request that the Examiner withdraw this rejection of claims 21-31.

REJECTION UNDER 35 U.S.C. § 112, 2ND PARAGRAPH

The Examiner rejected claims 11 and 12 as allegedly indefinite because they fail to define what IL-1 activity Applicants intended to block. Claims 11 and 12 have been amended to recite that the BMP blocks the IL-1 effect on cartilage growth. This amendment finds support in the specification at page 27, lines 15-28. Applicants respectfully request that the Examiner withdraw this rejection of claims 11 and 12.

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

Dated: 1/20/04

By: Elizabeth McNamee
Elizabeth E. McNamee
Reg. No. 54,696

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com